Department of Tropical Medicine

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General Summary

There is a great need to develop novel parasite control strategies because of the failures of current eradication approaches and the logistical difficulties to implement them. One interesting aspect of these diseases is that the vector arthropods that transmit the pathogens can mount immune responses against the infection that will kill a large proportion of parasites. Our group is pursuing research that covers 4 topics: (1) vector–parasite interactions, (2) infection response in intermediate host, (3) immune responses to helminth infection, and (4) vector epidemiology.

Research Activities

Dissection of blood sucking behavior of mosquitoes

Exploring the molecular mechanism of blood sucking behavior of female mosquitoes is one of the critical steps to fight against vector–borne disease such as dengue and malaria, since pathogens are transmitted when mosquitoes are gorging on blood. Recently, it was reported that the expression of one gustatory receptor, Gr5 is significantly higher in labella (tip of proboscis) of female Aedes aegypti compared to that of male in RNAseq analysis. Since only female mosquitoes take blood meal and gustatory receptors are generally involved in the perception of taste, we hypothesized that Gr5 might contribute to perceive the blood taste. When we generated Gr5 mutants by CRISPR/Cas9 system, Gr5 mutants showed defects in starting the ingestion of blood, although they did not show defects in host searching and probing behavior. Thus, Gr5 is indicated to regulate the initiation of blood ingestion. We would like to reveal the ligand for Gr5 and neurons that express Gr5, and these findings will give us important insights into the blood sucking behavior of mosquitoes.

Elucidation of molecular basis of tick host detection

Tick–borne diseases present major public health issues worldwide. In ticks, the development of larvae and nymphs and the production of eggs by adults are all dependent on the acquisition of nutrients from the host blood–meal. Only one blood–meal is taken during each life stage and ticks can survive for several months after completion of feeding without requiring a further blood–meal. However, the precise mechanism responsible for host recognition is unknown. Recently, evidence for thermosensitive sensilla on mosquito appendages has been uncovered. It was reported that the activation of a transient receptor potential, via ion channels involved in various types of sensory reception, including thermo–, chemo–, mechano–, and photoreception, is caused by an increase in temperature from 25°C to 37°C in mosquitoes. We investigated the moleculer characterization of the thermosensitive transient receptor potential channel (TRPA1) identified in the hard tick

Haemaphysalis longicornis. The transient receptor was found be expressed at highest levels in legs, chelicera and midgut of H. longicornis. Immunolocalization studies detected the endogenous TRPA1 in legs and chelicera of an adult tick. We will investigate the participation of TRPA1 molecules in host exploratory behavior by the behavior analysis system. We will investigate the participation of TRPA1 molecules in host exploratory behavior by the behavior analysis system.

Toward the establishment of more suitable strain of Lucilia sericata for maggot debridement therapy

Maggot debridement therapy (MDT) is an effective method for debriding wounds such as leg ulcers, supporting wound bed preparation. The larvae of the sheep blowfly, Lucilia (Phaenicia) sericata are the most widely used species for MDT due to its preference for feeding on necrotic tissues over healthy. New evidences have been emerging to suggest that maggots might contribute to wound healing in other ways such as reduction of biofilms and disinfection of wounds and stimulating the growth of healthy tissue. In this study, several new strains for L. sericata were screened and established toward developing a maggot strain for more efficient MDT. Wild fly larvae were collected from total 43 corpses during forensic autopsies and raised to adults to establish laboratory-reared lines. Larvae of each strain fed on human tissues, which were prepared from surgical debridement, were examined for food consumption, body weight, and growth rate, compared to the conventional L. sericata strain for MDT. One of the corpse-borne strains (No. 28) showed the most favorable outcomes in all three evaluation points, suggesting more efficient debridement in MDT with this new strain.

Resident CD4+ memory T cell-derived interleukin-3 play a crucial role in basophil recruitment to tick-feeding site for acquired anti-tick immunity

Blood-sucking arthropods serve as vectors for infectious disease transmission. Ticks transmit medically important diseases such as Lyme borreliosis. In several animals, resistance to subsequent infestations after the primary infestation of ticks has been reported. In a mouse model, basophils accumulate tick-feeding sites during the second but not first infestation, and play a significance role in the development of acquired tick resistance, although the mechanism remains unknown. We, herein, examined both cells and their products responsible for the recruitment. Little basophil accumulation was observed in T cell-deficient mice, and adoptive transfer of CD4+ T cells reconstituted it. Interleukin (IL)-3 gene expression was highly up-regulated at the second tick-feeding sites, and adoptive transfer of IL-3-sufficient but not-deficient CD4+ T cells conferred the basophil accumulation in T cell-deficient mice. This indicates CD4+ T cell-derived IL-3 is crucial for the basophil recruitment. Interestingly, before the second infestation, IL-3+ resident CD4+ with memory phenotype T cells were detected even in previously uninfested sites of skin that were distant from the primary infested site. These results indicate that IL-3 from resident skin CD4+ memory T cells seems to be essential for basophil recruitment to the second tick-feeding sites. This finding would be valuable for a vaccine strategy against infectious diseases transmitted by blood-sucking arthropods.

Publications

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